IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY

SYMED LABS LIMITED and HETERO USA, INC., Plaintiffs, v. ROXANE LABORATORIES, INC., Defendant	Civil Action No.: 2:15-cv-08304-CCC-MF ***(LEAD DOCKET)***
SYMED LABS LIMITED and HETERO USA, INC., Plaintiffs, v. GLENMARK PHARMACEUTICALS INC., Defendant	Civil Action No. 2:15-cv-08306–CCC-MF
SYMED LABS LIMITED and HETERO USA, INC., Plaintiffs, v. AMNEAL PHARMACEUTICALS LLC, Defendant	Civil Action No. 2:15-cv-08307–CCC-MF

SECOND DECLARATION OF JERRY L. ATWOOD IN SUPPORT OF PLAINTIFFS' RESPONDING CLAIM CONSTRUCTION BRIEF

TABLE OF CONTENTS

EXHIBITS

I, Jerry L. Atwood under penalty of perjury declare as follows:

A. INTRODUCTION

1. I submit this declaration as a technical expert in support of the Responsive Claim Construction Brief submitted concurrently with this declaration by Plaintiffs Symed Labs Limited and Hetero USA Inc.

2. My qualifications and experience have been set forth in my first Declaration already submitted in support of Plaintiffs' Opening Claim Construction Brief on March 6, 2017. The present declaration supplements my original Declaration. I use the same abbreviations herein and I rely on some of the same documents. The opinions expressed herein are valid as of the present time and would also have been valid as of October 16, 2003, the filing date of the Patents-in Suit (defined below).

B. PURPOSE AND SUMMARY OF OPINION

3. I submit this declaration to establish that certain positions taken by Defendants in Defendants' Opening Claim Construction Brief and certain information provided and opinions expressed in the Declaration of Dr. Robin D. Rogers submitted in support of Defendants' Opening Construction Brief are not well-taken and/or are not accurate and/or are not applicable to the situation at hand.

4. In preparation for submitting this declaration, I have reviewed the Defendants' Opening Claim Construction Brief and the accompanying Declaration of Dr. Robin D. Rogers. I have also again reviewed U.S. Patents 7,714,128; 7,718,799; and 7,732,597 (collectively, "the Patents-in-Suit") as well as portions of their prosecution histories. I have also reviewed a number of other documents, both patents and technical literature, such as those I cite in this declaration.

5. More specifically, first, I submit this declaration to show that a person of ordinary skill in the art ("POSA") would have no trouble ascertaining the meaning of the phrase appearing in the Patents-in-Suit "characterized by an X-ray powder diffraction spectrum having peaks expressed as 2θ at about 7.6, 9.6, 13.6, 14.9, 18.2, 18.9, 21.2, 22.3, 25.6, 26.9, 27.9 and 29.9 degrees." With respect to the XRPD spectrum peaks recited in the claim, the appropriate margin of error for the scattering angles 2θ of the twelve strongest

reflections obtained for an analyte is within ± 0.20 degrees of that of the claimed reference material in the absence of the word "about." The word "about" in that phrase serves to account for the additional possibility that a small number of peaks might be slightly outside that margin compared to the claimed peaks. However, as I have stated in my original Declaration and as I will show below, this does not detract from the ability of a person of ordinary skill in the art ("POSA") to ascertain readily whether a given linezolid material is or is not within the claim, *i.e.*, is or is not the claimed Form III.

6. Second, I submit this declaration to show that a person of ordinary skill in the art would not interpret the statement in the prosecution history of U.S. Patent 7,714,128 ("the '128 Patent") relied on by the Defendants as modifying the foregoing margin of error from ± 0.20 to ± 0.10 degrees 2θ. This is so especially in view of other statements in which the appropriate margin, ± 0.20 degrees 2θ, is invoked and which were made by Plaintiff Symed in the prosecution of the same application or in another application in the same patent family. Accordingly, I have concluded that the smaller margin of error was simply a mistake and, in my opinion, a POSA after review of the entire prosecution history, would reach the same conclusion.

7. Third, I submit this declaration, to show that a POSA contemplating the claimed feature of "an IR spectrum having main bands at about 3338, 1741, 1662, 1544, 1517, 1471, 1452, 1425, 1400, 1381, 1334, 1273, 1255, 1228, 1213, 1197, 1176, 1116, 1082, 1051, 937, 923, 904, 869, 825 and 756 cm-1" would similarly not have trouble ascertaining what the phrase means. The data points or bands included in the phrase would have implicitly associated with them an appropriate margin of error which in the literature is given as ± 0.1 – 10 cm^{-1}. Second, I submit this declaration to show that a POSA would similarly, consider the word "about" to modify slightly the foregoing margin of error inherent in determining the IR spectra and to account for example for the masking of some of the data points which may occur depending on the procedure used. Despite this, however, the nature of the substance and its polymorphic form can be determined as investigators (*i.e.*, POSA) have already done even when the method by which the IR spectra were generated was not the same. This would be all the more so if a POSA contemplating the claimed IR bands already had access to XRPD spectra for linezolid Form III or the form being tested (as the claims of the Patents-in-Suit require).

8. Fourth, I also submit this declaration to show that with regard to an IR study a POSA would readily realize that, of the two commonly used methods of sampling, employing the potassium bromide (KBr) method (which is also *the* most common method) should be used for linezolid. The other commonly used method employs mull oil. However, several of the bands recited in the claim are such that the bands will be obscured if mull oil is used. Even though it is still possible to determine the crystal form of a sample, especially when also having the benefit of its XRPD spectra, a POSA would not choose an analytical method that would be expected to mask some of the results. Rather, a POSA would use the KBr method to generate IR data.

9. My overall conclusion is that the meaning of the claims is easily ascertainable by a person of ordinary skill in the art

C. ± 0.2 DEGREES 2θ: THE MARGIN OF ERROR IN THE XRPD SPECTRA OF THE PATENTS IN SUIT

10. As I stated in my original Declaration, as of October 16, 2003, the date the Patents-in-Suit were filed, the widely accepted margin of error between reference XRPD peaks and experimentally determined XRPD peaks was ± 0.2 degrees 2θ. The Rogers Declaration does not speak to this point. In my view, the word "about" modifies and slightly broadens this accepted margin of error implied in the XRPD peak values of the claims of the Patents-in-Suit. In my original declaration, I concluded that this extra leeway afforded by "about" is an extra ± 0.1 degrees 2θ. I stand by that conclusion. I have read excerpts of the prosecution history of the '128 Patent and the '597 Patent from the point of view of a POSA to see whether Symed has said anything that should be taken as a narrower margin and concluded that it does not. The instance relied on by the Defendants where an error margin of ± 0.1 instead of 0.2 is said to be adopted, is found in an Amendment dated February 5, 2008, in the prosecution history of the '128 Patent (Exhibit A, at p. 4). On the last line of the same page, the same Amendment mentions a margin of error of 0.2 degrees which corresponds to the generally accepted one (although it is missing the ± sign). This leads me to understand that "0.1 degrees" is simply a mistake. There is no other mention of such a value in the specification of the Patents-in-Suit or in their prosecution histories. Furthermore, the statement is at best informational and I can

see no advantage to Symed in restricting the error margin implicit in the claimed XRPD peaks. Thus, I do not see this obviously erroneous acceptance margin as contributing to an elucidation of the meaning of the claims to a POSA.

12. More importantly, other instances in the same prosecution history point to the correct margin of error of ± 0.2 degrees 2θ, reinforcing my opinion that the instance pointed to by Defendants is simply an error. In a document entitled Request for Declaration of an Interference with an Application under 37CFR 41.02 (Exhibit B, submitted June 4, 2009) Symed sought to provoke an interference with Teva's Aronhime application (the latter attached as Exhibit E to my original declaration). At p. 4, Symed stated that the proposed "Count" (which I understand to be similar to a patent claim, but directed to claimed subject matter common to both applications) was as follows:

> A crystalline linezolid characterized by:
>
> (a) a powder X-ray diffraction pattern with peaks at about 7.5, 13.5, 18.0, 18.7, 19.9, 21.1, 22.2, 25.4, 27.7, and 28.4 ± **0.2 degree 2 theta**;
>
> OR
>
> (b) an FTIR spectrum with peaks at about 2817, 1335, 1229, 1200, and 662 cm-1,
>
> wherein there is at least a 99.8% enantiomeric excess of the linezolid form III.

Symed went on to say that Claim 1 and Claim 39 of the Symed Application "corresponded" to the proposed Count. I understand this to mean that Claim 1 of the Symed application (which was identical to that issued as Claim 1 of the '128 patent) contained the same necessary features as the count, including the ± 0.2 degree 2 theta error margin.

13. In yet another excerpt of the prosecution history of the Patents-in-Suit, inventor Dr. D. Mohan Rao stated in a declaration (*i.e.*, a verified statement) that the crystal form of linezolid obtained by the process claimed in that particular patent application (which ultimately issued as the '597 Patent) was the same as that described in the specification

and was claimed in terms of its XRPD peaks (which was obtained by a different process), *i.e.*, was Form III. Exhibit C, titled "Declaration of D. Mohan Rao, Ph.D. under 37 CFR 1.132" (executed November 21, 2009). In the Declaration, Dr. Rao describes experiments wherein the measured XPRD data for the claimed linezolid Form III was in agreement within a margin of ± 0.2 degrees 2θ, as well as experiments wherein linezolid made by the process claimed in the application wherein the declaration was submitted was also in agreement with the claimed XRPD data with a margin of ± 0.2 degrees 2θ. See Appendix 1-D of Exhibit C. I note that one set of values, claimed as 14.9 degrees 2θ, was measured as 14.8 degrees 2θ and as 14.6 degrees 2θ, the latter being 0.3 degrees 2θ from the corresponding claimed value. Based on this comparison, Dr. Rao concluded that the crystalline linezolid produced by either process was the same as the claimed Form III. (Exh. __ at p. 3). I concur with this opinion. Clearly, Dr. Rao (who is also an inventor) understood that the peak measured as 14.6 degrees 2θ was, in fact, the peak claimed as 14.9 degrees 2θ. Similar discrepancies can be seen in Appendix 1-F of the same Rao declaration.

14. Lastly, investigators at Teva Pharmaceutical Sciences, have determined that a form of linezolid that they originally believed was a new form (Form IV) is in fact identical to Form III. See, Teva's International (PCT) Application WO 2007/018588 ("Teva's '588 Application," Exhibit D) which admits that the two forms are identical on the basis of XRPD spectra wherein several of the peaks differ by 0.2 degrees 2θ. Compare p. 3, lines 4 – 9 of Teva's '588 Application which repeats the claimed set of XRPD peaks (and which contains an acknowledgement of identity) to p. 21, lines 4 – 7 of the same document which reports the XRPD peaks for Teva's product.

D. ± 0.1 – 10 cm^{-1}: THE ACCEPTED MARGIN OF ERROR IN THE IR SPECTRA OF THE PATENTS IN SUIT

15. In my opinion, the phrase in the claims of the Patents-in-Suit "characterized by an IR spectrum having main bands at about 3338, 1741, 1662, 1544, 1517, 1471, 1452, 1425, 1400, 1381, 1334, 1273, 1255, 1228, 1213, 1197, 1176, 1116, 1082, 1051, 937, 923, 904, 869, 825 and 756 cm-1" would have an error range associated with it: the widely reported ± 0.1 cm^{-1} – 10 $cm.^{-1}$ · U.S. Pharmacopoeia 37 Gen'l Ch. 851 (Exhibit E) which depends on the instrument used. I observe that the range is wide but, in my view, it is not

unreasonable. As I discuss in more detail in the next Section, in reference to experiments conducted by a POSA and available in the patent and technical literature, relatively large discrepancies are encountered in linezolid data and yet a POSA would have no trouble confirming the identity of a linezolid crystal form or distinguish between two different crystal forms of linezolid even when the samples are prepared and handled by different methods.

16. A comparison of the IR bands claimed in the Patents-in-Suit and those from three independent third-party IR measurements of Form III linezolid are given in Exhibit L. The largest difference in wavenumber for any bands in these four measurements is 9 cm^{-1} for the claimed band at 1741 cm^{-1} and that measured by Aronhime, 1732 cm^{-1}. Therefore, the widely reported error range of 10 cm^{-1} has been verified for the four measurements of the infrared spectrum of Form III linezolid.

17. Accordingly, I cannot agree that the meaning of this phrase could not be ascertained by a POSA as of the filing date of the Patents-in-Suit, October 16, 2003.

E. ABILITY OF POSA TO DETERMINE WHETHER A LINEZOLID POLYMORPH IS ENCOMPASSED BY THE CLAIMS OF THE PATENTS IN SUIT.

18. Dr. Rogers states in his declaration that the specification of the Patents-in-Suit is defective, causing the claims to be indefinite, because it does not specify which method was used to prepare the sample for IR testing. In my opinion, a POSA contemplating the claims which call for "an IR spectrum having main bands at about 3338, 1741, 1662, 1544, 1517, 1471, 1452, 1425, 1400, 1381, 1334, 1273, 1255, 1228, 1213, 1197, 1176, 1116, 1082, 1051, 937, 923, 904, 869, 825 and 756 cm-1" would readily realize that, of the two commonly used methods used to generate IR spectra, the method employing potassium bromide (KBr pellet) (which is also the most common method) should be used for linezolid. The other commonly used method employs mull oil (Nujol being a trade name for a commonly used mull oil) alone. Sample preparation techniques for both KBr pellet and mull oil methods are described simply and clearly in IR Sample Preparation: A Practical Guide, Derry, P. and Barron, A. R., copy attached as Exhibit F . This guide teaches proper sample preparation and handling.)

19. The reason I believe that a POSA would readily conclude that the IR spectra recited in the patent were generated using the KBr method is that the claims include several bands between wavenumbers 1471 and 1382 cm^{-1} which fall in a portion of the spectrum where mull oil has very intense bands. A POSA would therefore opt for the KBr method in order to avoid linezolid bands being obscured by mull oil bands.

20. As noted above in paragraph 16, a group of investigators generated linezolid IR spectra using both the KBr method and the mull oil (Nujol) method. Wielgus, E. *et al.*, *J. Pharm. Sci.*, **104**: 3883-3892 (2015) including its Supporting Information, particularly p. S7 (both attached as Exhibit G). Using the data of Wielgus *et al.* and the IR values in the Patents-in-Suit, I created the following Exhibits:

21. Exhibit H (titled "Form III patent v. Form III Wielgus") contains a comparison table on its page 1 of the claimed IR spectra for Form III (left column) with that generated by Wielgus *et al.* using each of KBr (middle column) and mull oil (Nujol) method (right column). It can be clearly seen that in the Nujol method there are no peaks between wavenumbers 1471 and 1381 cm^{-1}. For the KBr method, the band at 1424 cm^{-1} is listed. (Note that the Wielgus KBr pellet method does not have as many bands as does the Nujol method. This is clearly due to the use of less sample in the KBr pellet.) On page 2 of Exhibit __, I have provided a copy of the Nujol IR spectrum from the literature. Nujol displays two very large bands and a smaller but still substantial band between wavenumbers 1280 and 1500 cm^{-1} on this spectrum, explaining the missing linezolid Form III bands in the corresponding wavenumber range in the comparison table on p. 1.

22. On p. 1 of Exhibit H, it can be seen that several bands of the data generated by Wielgus for Form III using the KBr pellet method differ in wavenumber by 1 to 3 cm^{-1}. This is attributed to the built-in experimental error. The number of bands reported as significant by Wielgus was also smaller than that of the claims. This smaller number was still sufficient to permit the Wielgus *et al.* authors to identify the material as linezolid Form III.

23. Exhibit I (titled "Form III Patent v. Form II Wielgus") shows on p. 1 that there is close agreement (a difference below 10 cm^{-1}) between many of the wavenumber values of the two forms but that there are four bands (the top one at 3338/3362 cm^{-1}, the third from the top at 1662/1675 cm^{-1}, the one at 1176/1144 cm^{-1} and the one at 869/851 cm^{-1}) which

differ by more than 10 cm^{-1}, precluding the authors, and more generally a POSA, from misreporting Form II as Form III.

24. Similarly, Exhibit J (titled "Form III Patent v. Form I Background of Patent") confirms that all bands attributed to Form I as reported in the '128 Patent except one differ from the values claimed for Form III by more than 10 cm^{-1}. In my view this amply supports the conclusion that Form I and Form III are different. This Exhibit complements the foregoing exhibits based on the work done by Wielgus.

25. There is another example where a POSA was able to confirm the identity of the crystal form of two different linezolid samples even if several points differ by as much as 10 cm^{-1}. Compare the IR spectra determined by Teva (using the mull oil method) in the Aronhime patent application (Exhibit E to my original declaration) with the claimed IR bands in the Patents-in-Suit (which were generated using the KBr method). I have duplicated these data in Exhibit L. The ability of a POSA to establish identity is aided by the co-presence of matching XRPD spectra. But the claims of the Patents-in-Suit call for the IR spectra as a confirmatory feature in addition to the XRPD spectra. As a result, a POSA would not have trouble determining if a given sample contains a linezolid polymorph that is within the claim.

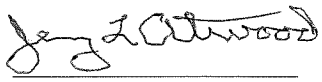
26. Accordingly, Dr. Rogers' opinion (if an error margin of up to $\pm$ 10 cm^{-1} were used, the values of different polymorphic forms would be conflated, not permitting them to be distinguished from one another) is not borne out. To the contrary, a POSA would have distinguished among different linezolid forms (or confirmed that they are the same).

27. Indeed, a POSA would have been able to confirm or distinguish linezolid crystal form not only when using the same method but also when using different sample preparation methods. For example, in the file history of the '128 Patent. Symed attempted to provoke an interference with the Aronhime Application of Teva (US 2006/0142283, copy attached as Exhibit E to my original Declaration). Symed's Dr. Rao was able to establish identity between the IR pattern of the so-called Form IV in the Aronheim Application and Linezolid Form III. See Second Rao Declaration dated June 3, 2009 (Exh. K), and specifically its Appendices 2-C and 2-D.

28. In summary, the sample and technique used to analyze linezolid in the Patents-in-Suit and to reach conclusions about the crystal form of linezolid involved would be clear

to a POSA. Actual investigators have not had any difficulty identifying Form III by comparing their IR data to the claimed values and distinguishing it from Form II. Similarly, clear distinctions exist between Form III and Form I, permitting a POSA to distinguish between these forms.

Dated May 15, 2017



Jerry L. Atwood